

We claim:

Sub A

1. A method to modulate angiogenesis comprising administering to an individual in need of treatment thereof an effective amount of a chondroitin sulfate degrading enzyme.

5 2. The method of claim 1 wherein the enzyme is selected from the group consisting of bacterial glycosaminoglycan degrading enzyme and is selected from the group consisting of chondroitinase-AC from *Flavobacterium heparinum*, chondroitinase B from *Flavobacterium heparinum*, chondroitin sulfate degrading enzymes from *Bacteroides species*, chondroitin sulfate degrading enzymes from *Proteus vulgaris*, chondroitin sulfate degrading enzymes from *Micrococcus*, chondroitin sulfate degrading enzymes from *Vibrio species*, chondroitin sulfate degrading enzymes from *Arthrobacter aureus*, arylsulfatase B, N-acetylgalactosamine-6-sulfatase and iduronate sulfatase from mammalian cells, all of these enzymes expressed from recombinant nucleotide sequences in bacteria and combinations thereof.

15 3. The method of claim 1 wherein the enzyme is a mammalian enzyme.

4. The method of claim 1 wherein the enzyme is a chondroitinase.

20 5. The method of claim 4 wherein the chondroitinase is chondroitinase AC.

6. The method of claim 1 wherein the individual has cancer.

7. The method of claim 6 wherein the cancer is a solid tumor and the enzyme is chondroitinase AC.

25 8. The method of claim 1 wherein the individual has a disorder in which angiogenesis is involved, the disorder being selected from the group consisting of rheumatoid arthritis; psoriasis; ocular angiogenic diseases, rubeosis; Osler-Webber Syndrome; myocardial angiogenesis; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; disease of excessive or abnormal stimulation of endothelial cells, Crohn's disease, 30 atherosclerosis, scleroderma, and hypertrophic scars, diseases that have

in paper marked group - need specific enzymes, not a specific factor in group claim.

Sub C2

Sub C3

Sub B2

Sub C5

angiogenesis as a pathologic consequence, adhesions, scarring following transplantation, cirrhosis of the liver, pulmonary fibrosis following acute respiratory distress syndrome or other pulmonary fibrosis of the newborn, endometriosis, polyposis, obesity, uterine fibroids, prostatic hypertrophy, and amyloidosis.

9. The method of claim 1 wherein the enzyme is administered systemically.

10. The method of claim 1 wherein the enzyme is administered topically or locally at or adjacent to a site in need of treatment.

11. The method of claim 1 wherein the enzyme is administered in a controlled and/or sustained release formulation.

12. A formulation for administration to an individual in need of treatment thereof for a disorder involving angiogenesis, the formulation comprising an effective amount of a chondroitin sulfate degrading enzyme to inhibit angiogenesis, wherein the dosage is different than the amount effective for wound healing, and a pharmaceutically acceptable carrier.

13. The formulation of claim 12 wherein the enzyme is selected from the group consisting of bacterial glycosaminoglycan degrading enzyme and is selected from the group consisting of chondroitinase AC from *Flavobacterium heparinum*, chondroitinase B from *Flavobacterium heparinum*, chondroitin sulfate degrading enzymes from *Bacteroides* species, chondroitin sulfate degrading enzymes from *Proteus vulgaris*, chondroitin sulfate degrading enzymes from *Micrococcus*, chondroitin sulfate degrading enzymes from *Vibrio* species, chondroitin sulfate degrading enzymes from *Arthrobacter aurescens*, these enzymes expressed from recombinant nucleotide sequences in bacteria and combinations thereof.

14. The formulation of claim 12 wherein the enzyme is a mammalian enzyme.

15. The formulation of claim 12 wherein the enzyme is a chondroitinase.

16. The formulation of claim 15 wherein the chondroitinase is chondroitinase AC.

17. The formulation of claim 12 wherein the enzyme is in a controlled, sustained release formulation.

5 18. The formulation of claim 12 in a dosage effective to inhibit angiogenesis and thereby inhibit or kill tumors.

*add
B3*

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